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(54) Membrane and process for producing the membrane.

(57) Membrane in the form of a flat sheet, tube, or hollow fiber having a hydraulic permeability to water of 10 −100 ml/m²/h/mmHg, and having a diffusive permeability to chloride (Cl^-) of more than 10 cm·sec × 10^{-4}, preferably more than 12 cm/sec × 10^{-4}, a diffusive permeability to vitamin B_{12} of more than 2 cm/sec × 10^{-4}, preferably more than 3 cm/sec × 10^{-4}, and a diffusive permeability to inulin of more than 0.5 cm/sec × 10^{-4}, preferably more than 1.0 cm·sec × 10^{-4}.

The membrane is prepared in a process involving the combined use of a high molecular weight swelling agent in the casting solution and partial evaporation of solvent prior to subjecting the membrane to gelling.

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TITLE

MEMBRANE AND PROCESS FOR PRODUCING THE MEMBRANE

TECHNICAL FIELD

This invention relates to a flat sheet, a tubular, or a hollow fiber membrane which is particularly, though not exclusively, suitable for use in so-called simultaneous hemodialysis/hemofiltration.

Furthermore, the invention relates to a process for producing this membrane, according to which a polymer solution is cast, extruded, or spun in the form of a flat sheet, a tube, or a hollow fiber which is gelled and, subsequently, washed and dried.

The invention will be described with particular reference to the so-called simultaneous hemodialysis/hemofiltration, but it should however already now be noted that the present membrane in its broad aspect is not restricted to only this particular use. It may as well be used in normal hemodialysis as in normal hemofiltration, and generally speaking, it may be used whenever it is intended or desired to separate a solute from a solution irrespective of whether this sepration is carried out by diffusive or convective solute transport through the membrane, as will be apparent from the following description.

TECHNICAL BACKGROUND

To be suitable for use in so-called simultaneous hemodialysis/hemofiltration, for which use the present membrane is particularly adapted, a membrane should be not only highly hydraulic permeable, but should also and simultaneously have high diffusive as well as high convective permeabilities to solutes to be separated. In

other words, such a membrane should as much as possible have the membrane characteristics of a hemodialysis membrane and a hemofiltration membrane at one and the same time.

As examples of known hemodialysis membranes may be mentioned the membranes described in for example the U.S. Patents Nos, 4 069 151, 4 075 108, and 4 308 145, and as examples of known hemofiltration membranes may be mentioned the membrane described in for example European Patent Publication No. 0 046 816.

An object of the present invention is thus to provide a membrane which has the combined membrane characteristics of a hemodialysis membrane and the hemofiltration membrane and which is therefore particularly, though not exclusively, suitable for use in so-called simultaneous hemodialysis/hemofiltration.

A further object is to provide a process for producing this membrane.

These and still further objects are achieved by means of the membrane and the process as defined in the accompanying claims 1 and 6, respectively, and which will be further illustrated in the following description.

BRIEF DESCRIPTION OF THE INVENTION

According to the present invention there is thus provided a flat sheet, a tubular, or a hollow fiber membrane which is particularly, though not exclusively, adapted for use in connection with so-called simultaneous hemodialysis/hemofiltration. The membrane is characterized by having a hydraulic permeability to water (ultrafiltration rate) of between 10 and 100 $ml/m^2/h/mmHg$, preferably 30 - 50 $ml/m^2/h/mmHg$, and by having a diffusive permeability to chloride (Cl^-) of more than 10 cm/sec x 10^{-4}, preferably more than 12 cm/sec x 10^{-4}, a diffusive permeability to vitamin B_{12} of more than 2 cm/sec x 10^{-4},

preferably more than 3 cm/sec x 10^{-4}, and a diffusive permeability to inulin of more than 0.5 cm/sec x 10^{-4}, preferably more than 1.0 cm/sec x 10^{-4}.

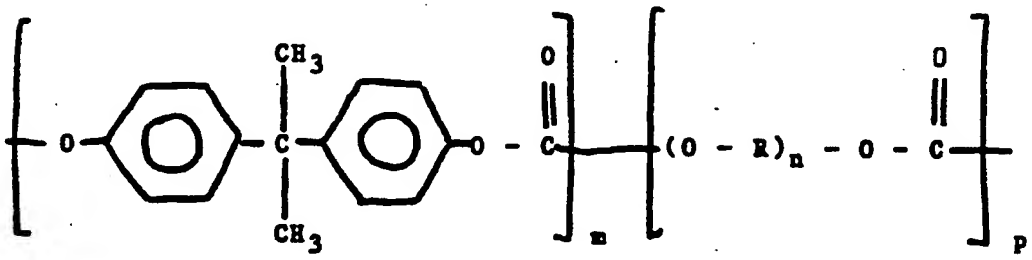
According to the present invention there is also provided a process for producing a flat sheet, a tubular, or a hollow fiber membrane which is particularly, though not exclusively, adapted for use in so-called simultaneous hemodialysis/hemofiltration, according to which a polymer solution is cast, extruded, or spun to produce a flat sheet, a tube or hollow fiber which is gelled and subsequently washed and dried. The process is characterized in that said polymer solution is containing a high molecular weight swelling agent and in that the extruded flat sheet, tube, or hollow fiber is exposed to partial evaporation of solvent prior to said gelling.

DETAILED DESCRIPTION OF INVENTION

The cut-off value of the membrane can be set at any predetermined value depending on the intended use of the membrane. When the membrane is intended for use in extracorporeal treatment of blood it is however desired to set the cut-off such that toxic uremic substances (metabolites) will freely pass through the membrane, while for example albumin (M_w = 68 000 Daltons) is retained. A preferred cut-off value is about 50 000 Daltons.

According to the invention the membrane may be prepared from a polymer chosen among polycarbonate block copolymers such as polyether-polycarbonate block copolymers and organopolysiloxane-polycarbonate block copolymers. Further examples of usable polymers for the present membrane may be polyacrylonitriles as well as modified polyacrylonitriles such as sulfonated polyacrylonitrile.

The most preferred polymer is a polyether-polycarbonate block copolymer, preferably a bisphenol A/polyalkylene oxide polycondensate containing 5 - 35% by weight of polyalkylène oxide, preferably 20%, and having the general formula



wherein R is designating CH_2CH_2, $CH_2-CH(CH_3)$ or combinations of CH_2-CH=CH and CH=CH, preferably CH_2CH_2, m and p are chosen such that the bisphenol A carbonate unit is about 95 to 65% of the weight of the recurring unit and the alkylene oxide unit is about 5 to 35% of the weight of the recurring unit, and wherein n = 10 - 220, preferably 182.

The thickness of the present membrane may vary within wide limits and is usually within the range of from 10 to 60 µm. A preferred thickness is 25 - 45 µm.

As suggested hereinabove, it is essential in the process according to the present invention to combine the use of a high molecular weight swelling agent (to form a highly water and solute permeable porous structure) and partial evaporation of solvent (to form a denser layer which restricts the permeability of the membrane to solutes) prior to gelling the extruded membrane.

By the term "high molecular weight" swelling agent in accordance with the present invention is meant swelling agents having a molecular weight within the range of from 1 000 to 20 000 Daltons. A preferred molecular weight range is from 3 000 to 15 000 Daltons.

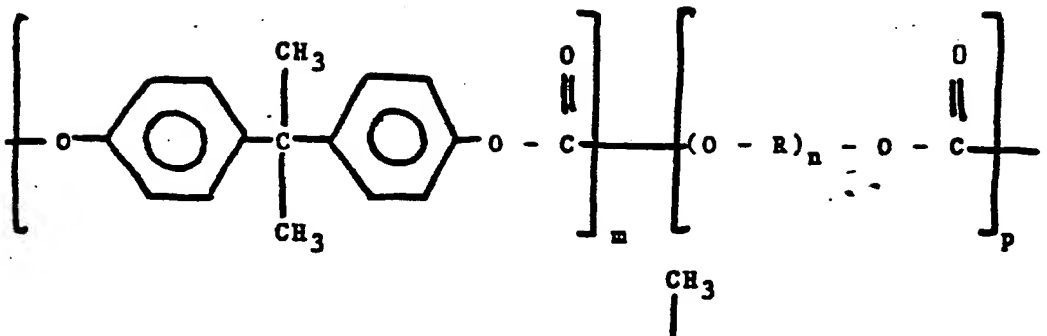
Examples of such high molecular weight swelling agents are polyethylene glycols, preferably a polyethylene glycol having a molecular weight of 8 000 Daltons, and polypropylene oxide-polyethylene oxide block copolymers, such as Pluronic F 68 (BASF Wyandotte). Further examples may be dextran, inulin and polyvinylpyrrolidone.

Suitable high molecular weight swelling agents in accordance with the present invention are however not restricted to the above-mentioned swelling agents, but any known swelling agent which has a high molecular weight, as defined hereinabove, being soluble in the polymer solution, and being removable in the gelation bath could be used.

According to the present invention such high molecular weight swelling agents are in general used in amounts ranging from 1 up to 8% by weight in the polymer solution (casting or spinning solution). Preferably, they are used in amounts of 2 - 5% by weight.

Suitable polymers to be used in the process according to the present invention may be chosen among polycarbonate block copolymers such as polyether-polycarbonate block copolymers and organopolysiloxane-polycarbonate block copolymers. Further examples of suitable polymers may be pilyacrylonitriles and modified polyacrylonitriles such as sulfonated polyacrylonitrile.

The most preferred polymer is however a polyether-polycarbonate block copolymer, preferably a bisphenol A/polyalkylene oxide polycondensate containing 5 - 35% by weight of polyalkylene oxide, preferably 20%, and having the general formula



wherein R is designating CH_2CH_2, CH_2-CH or combinations of CH_2-CH=CH and CH=CH, preferably CH_2CH_2, m and p are chosen such that the bisphenol A carbonate unit is about 95 to 65% of the weight of the recurring unit and the alkylene oxide unit is about 5 to 35% of the weight of the recurring unit, and wherein n = 10 - 220, preferably 182.

The polymer solution is generally formed to have a viscosity within the range of from 4 000 to 50 000 cPs. A preferred viscosity range is 18 000 - 25 000 cPs.

The present invention will be further illustrated by means of the following examples.

Example 1

A filtered polymer solution, prepared from 85.7% by weight of dioxolane, 12.25% by weight of polyether-polycarbonate block copolymer, and 2.05% by weight of polyethylene glycol (M_w = 3 400) with a viscosity of 18 000 cPs was extruded via a doctor blade onto a moving substrate. After evaporation of about 20% of the dioxolane, the extruded membrane was precipitated in a water bath, removed from the substrate, washed free of dioxolane and polyethylene glycol, stabilized in an ethanol/glycerol/water mixture, and dried with air.

The resultant membrane had the following properties:

Ultrafiltration rate: 21 $ml/m^2/h/mmHg$

Diffusive permeability to chloride: 13.0×10^{-4}cm/sec

B_{12} : 5.0×10^{-4}cm/sec

inulin: 0.8×10^{-4}cm/sec

Thickness: 28 µm

Example 2

A filtered polymer solution, prepared from 84.3% by weight of dioxolane, 12.1% by weight of polyether-polycarbonate block copolymer, and 3.6% by weight of polyethylene glycol (M_w - 8 000) with a viscosity of 20 000 cPs was extruded via a doctor blade onto a moving substrate. After evaporation of about 25% of the dioxolane the membrane was precipitated in a water bath, removed from the substrate, washed free from dioxolane and polyethylene glycol, stabilized in a glycerol/water mixture, and dried in warm air.

The resultant membrane had the following properties:

Ultrafiltration rate: 60 $ml/m^2/h/mmHg$

Diffusive permeability to chloride: 13.8×10^{-4} cm/sec

B_{12} : 5.2×10^{-4} cm/sec

inulin: 1.7×10^{-4} c,/sec

Thickness: 45 µm

Example 3

A filtered polymer solution, prepared from 86.6% by weight of dioxolane, 12.2% by weight of polyether-polycarbonate block copolymer, and 1.2% by weight of Pluronic F 68 (BASF Wyandotte) with a viscosity of 22 000 cPs was extruded via a doctor blade onto a moving substrate. After evaporation of about 20% of the dioxolane, the membrane was precipitated in a water bath, removed from the substrate, washed free of dioxolane and Pluronic F 68, stabilized in an ethanol/glycerol/water mixture, and dried with air.

The resultant membrane had the following properties:

Ultrafiltration rate: 13 $ml/m^2/h/mmHg$

Diffusive permeability to chloride: 12.1×10^{-4} cm/sec

B_{12} : 4.6×10^{-4} cm/sec

inulin: 1.7×10^{-4} cm/sec

Thickness: 28 µm

In the following table the effect of molecular weight of polyethylene glycol (PEG), used as swelling agent, on ultrafiltration rate of a membrane obtained in the process according to the present invention is illustrated.

Swelling agent/ Molecular weight	Ultrafiltration rate ($ml/m^2/h/mmHg$)
PEG 1540	9
PEG 3400	21
PEG 8000	50
PEG 18500	12
PEG 20000	9

The table shows the effect of equal amounts of polyethylene glycols of various molecular weight added to the polymer solution upon ultrafiltration rate of the obtained membrane. A maximum can be observed ror polyethylene glycol having a molecular weight of 8 000 Daltons.

INDUSTRIAL APPLICABILITY

The membrane according to the present invention is particularly, though not exclusively, suitable for use in so-called simultaneous hemodialysis/hemofiltrtion. It may as well be used in normal hemodialysis as in normal hemofiltration, and, generally speaking, it may be used whenever it is intended to separate a solute from a solution irrespective of whether this separation is carried out by diffusive or convective solute transport through the membrane.

CLAIMS

1. A flat sheet, tubular, or hollow fiber membrane which is particularly, though not exclusively, adapted for use in so-called simultaneous hemodialysis/hemofiltration, characterized by having a hydraulic permeability to water of between 10 and 100 $ml/m^2/h/mmHg$, preferably 30 - 50 $ml/m^2/h/mmHg$, and by having a diffusive permeability to chloride (Cl^-) of more than 10 cm/sec x 10^{-4}, preferably of more than 12 cm/sec x 10^{-4}, a diffusive permeability to vitamin B_{12} of more than 2 cm/sec x 10^{-4}, preferably of more than 3 cm/sec x 10^{-4}, and a diffusive permeability to inulin of more than 0.5 cm/sec x 10^{-4}, preferably of more than 1.0 cm/sec x 10^{-4}.

2. Membrane according to claim 1, characterized by having a cut-off value of 50 000 Daltons.

3. Membrane according to claim 1 or 2, characterized by being prepared from a polymer chosen among polycarbonate block copolymers such as polyether-polycarbonate block copolymers and organopolysiloxane-polycarbonate block copolymers; polyacrylonitriles; and modified polyacrylonitriles such as sulfonated polyacrylonitrile.

4. Membrane according to any of claims 1 - 3, characterized by having a thickness of 20 - 60 µm, preferably 25 - 45 µm.

5. Process for producing a membrane according to claim 1, wherein a polymer solution is cast, extruded, or spun to form a flat sheet, a tube or hollow fiber which is gelled and, subsequently, washed and dried, characterized in that said polymer solution is containing a high molecular weight swelling agent and in that the extruded flat sheet, tube, or hollow fiber is exposed to partial evaporation of solvent prior to said gelling.

6. Process according to claim 5, characterized in that said swelling agent has a molecular weight within the range of from 1 000 to 20 000 Daltons, preferably 3 000 -15 000 Daltons.

7. Process according to claims 5 or 6, characterized in that said swelling agent is used in an amount of from 1 to 8% by weight, preferably 2 - 5% by weight.

8. Process according to any of claims 5 - 7, characterized in that said swelling agent is chosen among polyethylene glycols, polypropylene oxide-polyethylene oxide block copolymers, dextran, inulin, and polyvinyl-pyrrolidone.

9. Process according to claim 8, characterized in that said swelling agent is a polyethylene glycol having a molecular weight of 8 000 Daltons.

10. Process according to any of claims 5 - 9, characterized in that said polymer is chosen among polycarbonate block copolymers such as polyether-polycarbonate block copolymers and organopolysiloxane-polycarbonate block copolymers; polyacrylonitriles; and modified polyacrylonitriles such as sulfonated polyacrylonitrile.

11. Process according to any of claims 5 - 10, characterized in that the polymer solution has a viscosity of from 4 000 to 50 000 cPs, preferably 18 000 - 25 000 cPs.